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EXAMINER	
LE, EMILY M	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/802,686	VAN NEST, GARY	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/12/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8-10 and 16-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-10 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/122006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/12/2006 has been entered.

Status of Claim(s)

2. Claims 6-7 and 11-15 are cancelled. Claim 18 is added. Claims 1-5, 8-10 and 16-18 are pending and under examination.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-5, 8-10 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue

experimentation. In Genentech *Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

Breadth of the claims:

The claims encompasses the administration of a oligonucleotide that is greater than 6 but less than 200 nucleotides in length, wherein the oligonucleotide comprises the CpG motif, in a subject that has been exposed to respiratory syncytial viral (RSV) infection to suppress the infection. The claims, with the exception of claim 5, are non-limiting to a particular oligonucleotide.

Nature of the invention:

The claimed invention is directed at the immunotherapeutic use of oligonucleotide comprising the CpG motif to stimulate the immune system, including the induction of Th1 immune response invoked by the production of Th1 associated cytokines accorded by the CpG motif, to suppress RSV infection in a subject that has been exposed to RSV.

Presence or absence of working examples:

The specification does contain working examples, however, it should be noted that none of them evidences that the administration of an oligonucleotide comprising the CpG motif suppresses RSV infection in a subject that has been exposed to RSV. The closes working examples provided are Examples 2-3.

Examples 2 demonstrates that the administration of an oligonucleotide comprising the CpG motif "on the day of infection was not effective." See lines 6-10, page 40 of Applicant's specification. In the same paragraph, Applicant also notes that the "administration before infection (in this experiment, 3 days) was effective at reducing viral titers. While the conclusion provided by Applicant is positive, however, it should be noted here that the claimed invention is directed at the suppression of RSV infection in subjects that has been exposed to RSV. That is, the subject must be exposed to RSV before the administration of an oligonucleotide to suppress RSV infectivity. It should further be noted that Example 2 is directed at the local administration, intranasal, of an oligonucleotide comprising the CpG motif, and that the claims, with the exception of claim 9, does not limit the method of administration to intranasal.

In addition to above, Example 2 provides that the administration of an oligonucleotide comprising the CpG motif does not suppresses RSV infection, see Table 1, disclosed on page 40 of the specification. Specifically, Table 1 provides that, like the control group, RSV is present in the lungs of test subjects that have been administered the oligonucleotide comprising the CpG motif. The data set forth in Table 1 clearly evidences that the administration of an oligonucleotide comprising the CpG motif does not suppress RSV infectivity in a subject, even when the oligonucleotide is administered prior to RSV infectivity.

Similar to Example 2, Example 3 is also directed at evaluating RSV viral titer in subjects. The difference between the two examples is that Example 2 uses a localized method of administration, intranasal; whereas, Example 3 employs a systemic method of administration, intraperitoneally and subcutaneously. Like Example 2, Example 3 sets forth that the systemic administration of an oligonucleotide comprising the CpG motif does not suppress RSV infectivity in the test subjects, as evidenced by Table 3. Table 3, disclosed on page 41 of the specification provides that, like the control group, RSV is present in the lungs of test subjects that have been administered the oligonucleotide comprising the CpG motif. The data set forth in Table 3 clearly evidences that the administration of an oligonucleotide comprising the CpG motif does not suppress RSV infectivity in a subject, even when the oligonucleotide is administered prior to RSV infectivity.

It should further be noted that, contrary to the conclusion provided by Applicant in Example 2, as supported by Table 2; Example 3 provides that the administration of an

oligonucleotide comprising the CpG motif was not effective at reducing viral titers, see Tables 4-5.

Furthermore, it should be noted that the working examples, Examples 2-3, are limited to the use of one very specific oligonucleotide, SEQ ID NO: 1. It should be noted that the claims, with the exception of claim 5, does not limit the oligonucleotide to those having the sequence set forth in SEQ ID NO: 1.

Amount of guidance or direction provided:

Aside from the stated teachings, i.e., Examples 2-3, the specification does not contain any additional guidance or direction that would enable the skilled artisan to practice the claimed invention without an undue burden of experimentation. All that is provided in the specification, with the exception of the working examples, is generic discussions of how to make oligonucleotides, methods of administration, treatment protocol, and the likes. The discussion is non-specific to the claimed invention. The specification does not teach an oligonucleotide comprising CpG motif that suppresses RSV infection in a subject infected with RSV.

State of the art:

The involvement of a Th1 type immune response in combating against intracellular pathogens is a well-recognized general concept. The art acknowledges the importance of Th1 type immune response, which is stimulated by the production of Th1 associated cytokines, in the elimination of intracellular pathogens, including viruses. However, the art has not accredited or recognized any one particular Th1-associated cytokine to the treatment, prevention and suppression of viral infection in a subject.

Specifically, the art teaches that while cytokines secreted by T helper cells are of critical importance for the outcome of many infectious diseases, the production of the "right" set of cytokines can be a matter of life or death, as noted by Infante-Duarte et al. Infante-Duarte et al. further notes that in addition to a Th1 type immune response, a Th2 type immune response is also necessary. Specifically, Infante-Duarte et al. teaches that a tight control over where and when Th1 and Th2 immune responses happen is necessary to keep intracellular infections under control, and to prevent the Th1 type immune response from causing damage to the host.[1] Hence, while the importance of a Th1 type immune response is well recognized in the art, the art further notes that a balance between Th1 and Th2 type immune responses is necessary to resolve an infection.

The cytokine art also provides that the efficacy of Th1 associated cytokines, such as interleukin 2, interleukin 12 and interleukin 18, against intracellular pathogens are controversial, as evidenced by Aoki et al.,[2] Bohn et al.,[3] Sakao et al.,[4] Zaitseva et al.,[5] and Masihi, K.[6] Aoki et al. teaches that while interleukin 2 may confer good protection for non-pathogenic mycobacterial strain Bacille Calmette-Guerin (BCG), interleukin 2 does not confer protection for virulent *M. bovis* infection. Bohn et al. teaches that

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[1] Infante-Duarte et al., Th1/Th2 balance in infection. Springer Seminars in Immunopathology, 1999, 21: 317-338. [Paragraph bridging pages 321-322, in particular.]
[2] Aoki et al. Use of cytokines in infection. Expert Opin. Emerg. Drugs, 2004, vol. 9, No. 2, 223-236. [Lines 4-15, left column, page 229,in particular]
[3] Bohn et al., Ambiguous role of interleukin-12 in Yersinia enterocolitica infection in susceptible and resistant mouse strains. Infect. Immune., 1998, Vol. 66, 2213-2220. [Abstract, in particular.]
[4] Sakao et al. IL-18-deficient mice are resistant to endotoxin-induced liver injury but highly susceptible to endotoxin shock. Int. Immunol., 1999, Vol. 11, 471-480. [Abstract, in particular.]
[5] Zaitseva et al. Interferon gamma and interleukin 6 modulate the susceptibility of macrophages to human immunodeficiency virus type 1 infection. Blood, 2000, Vol. 96, 3109-3117. [Abstract, in particular]

interleukin-12, a Th1 associated cytokine, induces different effector mechanisms that result in either protection or exacerbation of a disease. Specifically, Bohn et al. notes that the administration of exogenous interleukin 12 confers protection against Yersinia enterocolitica in susceptible BALB/c mice, but exacerbates yersiniosis in resistant C57BL/6 mice. Sakao et al. teaches that interleukin 18, a Th1 associated cytokine, is responsible for the progression of endotoxin-induced liver injury in mice primed with interleukin 18. Zaitseva et al. teaches that both interleukin 6 and interferon gamma augment the susceptibility of monocyte-derived macrophages to infection. Masihi, K. notes that interleukin 2 increases the production of HIV in vitro, and enhances the translocation of bacteria from intestines to other organs in animal studies. In summation, the art teaches that cytokines can be inherently toxic, have unclear pharmacological behavior and also have pleiotropic effects. Hence, the art recognizes that the use of cytokine to direct treatment is unpredictable and complicated.

Additionally, while the art teaches that oligonucleotides containing the CpG motif are capable of stimulating a Th1 type immune response, however, the art also teaches that the Th1 associated cytokine profile for these oligonucleotides vary from one oligonucleotide and species of subject to the next, as evidenced by Krieg et al. [7] and Mutwiri et al. [8] Krieg et al notes that each oligonucleotide containing the CpG motif must be considered as a separate agent because the quality and type of immune

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[6] Masihi, K. Fighting infection using immunomodulatory agents. Expert Opin. Biol. Ther., 2001, Vol. 1, No. 4, 641-653. [Lines 15-25, left column of page 646, in particular]

[7] Krieg et al., CpG motif in bacterial DNA and their immune effects. Annu. Rev. Immunol., 2002, Vol. 20, 709-760. [paragraph that bridge pages 716-717, in particular.]

[8] Mutwiri et al. Biological activity of immunostimulatory CpG DNA motifs in domestic animals. Veterinary Immunology and Immunopathology, 2003, Vol. 91, 89-103. [See 2nd and 3rd full paragraphs, left column of page 93; last sentence of paragraph bridging pages 89-90.]

stimulation induced by these oligonucleotides varies. Krieg et al. particularly notes that the type of cytokine stimulated by oligonucleotides containing the CpG motif is distinct from one oligonucleotide to the next. Additionally, both Krieg et al. and Mutwiri et al. note that the level and type of immune stimulation varies depending on i) the specific nucleic acids, purines and pyrimidines, surrounding the CpG motif; ii) the spacings between CpG motifs; iii) the numbers of CpG motifs in an oligonucleotide; iv) the absence or presence of a CpG motif to the end of the oligonucleotide; and v) the context in which the CpG motif is presented in the sequence.

The CpG art further teaches that the immunostimulatory activity of oligonucleotides containing the CpG is very species specific, as evidenced by Mutwiri et al. Table 1 of Mutwiri et al. provides that the *in vitro* immunostimulatory activity of oligonucleotides containing the CpG motif varies from one species to the next. Mutwiri et al. also notes that the level of immunostimulating induced by a particular oligonucleotide is also dependent on the sequence(s) flanking the CpG motif. Specifically, Mutwiri et al. notes that the GTCGTT motif, which is the optimal motif for humans, is optimal for stimulation of lymphocyte proliferation in several species including cattle, sheep, goats, horses, pigs, dogs, cats and chickens; whereas the murine CpG motif (GACGTT) is only optimal for inbred rabbits and mice.

Furthermore, both Krieg et al. and Mutwiri et al. sets forth that the recognition of the CpG motifs requires Toll-like receptor (TLR) 9, wherein cells that express TLR-9 produce Th1 associated cytokines. However, Mutwiri et al. provides that TLR-9 has only been identified in mice and humans. Mutwiri et al. also provides that the TLR-9 is

differentially expressed in humans and mice. Hence, if the recognition of the CpG motif were dependent of TLR-9, then it would logically follows that the extent of the Th1 type immune response induced by the oligonucleotide would necessarily vary from one species to the next. Mutwiri et al. also sets forth that *in vitro* observations do not accurately predict what happens *in vivo*.

Moreover, the potential use of oligonucleotides containing the CpG motif to stimulate a Th1 type immune response that treats, prevents and suppresses infection is widely speculated in the art. However, efforts to harness the immunostimulatory activity of oligonucleotides containing the CpG motif to trigger an innate immune response that protect a host from infectious pathogen has proven to be challenging and elusive, as evidenced by Yamamoto et al.,[9] Equils et al.,[10] Agrawal et al.,[11] and Olbrich et al.[12] Yamamoto et al. reports that oligonucleotides containing the CpG motif failed to improve the survival in mice challenged with influenza. Equils et al. teaches that such oligonucleotides can induce the HIV transcriptional regulatory elements in long terminal repeats, increasing viral replication. Agrawal et al. teaches that HIV-infected humans treated with oligonucleotides containing the CpG motif showed dose-dependent increases viral load. Lastly, Olbrich et al. teaches that the administration of oligonucleotides containing the CpG motif accelerated and increased the severity of Friend retrovirus in mice. In the case of Olbrich et al., the author notes that the use of

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[9] Yamamoto et al., Oligodeoxyribonucleotides with 5'ACGT-3' or 5TCGA-3 sequence induce production of interferons. Curr. Top. Microbiol. Immunol. 2000, Vol. 247, 23-40.
[10] Equils et al. Toll-like receptor 2 (TLR2) and TLR9 signaling resulted from HIV-long terminal repeat transactivation and HIV replication in HIV-1 transgenic mouse spleen cells: implications of simultaneous activation of TLRs on HIV replication. J. Immunol. 2003, 170, 5159-5164.
[11] Agrawal, et al. Was induction of HIV1 through TLR9? J. Immunol. 2003, 171, 1621-1621.

oligonucleotides containing the CpG motif for the treatment of viral infection may be a double edge sword that can resolute in effective therapy but also in acceleration of disease. Olbrich et al. notes that this double edge sword observation may be dependent on the time point of treatment.

Hence, overall, the literature notes the use of CpG to stimulate the production of cytokines, the use of cytokines to influence viral infection, and the development of a treatment regimen for diseases is unpredictable and complicated.

Predictability or unpredictability of the art:

As discussed above, the art recognizes that the use of cytokine to direct treatment is unpredictable and complicated. The art also recognizes that use of CpG to stimulate cytokine production, the use of the induced cytokine to influence viral infection, and the development of treatment regimen unpredictable and complicated. The art additionally teaches that the efforts to harness the immunostimulatory activity of oligonucleotides containing the CpG motif to trigger an innate immune response that protect a host from infectious pathogen has proven to be challenging and elusive.

Quantity of experimentation necessary:

Extreme undue burden of experimentation would be imposed upon the skilled artisan practicing the claimed invention. As stated above, Applicant has not provided much, if any, guidance or direction relating to the claimed invention. All that Applicant has provided is a conclusion that is made on the basis of generalized concepts that are well known in the art. And the formation of a conclusion based on generalized concepts

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[12] Olbrich et al. Preinfection treatment of resistant mice with CpG oligodeoxynucleotides renders them susceptible to friend retrovirus-induced leukemia. J. Virol., 2003, 77, 10658-10662.

renders the conclusion flawed. Generalized concepts are directed to support a general direction of studies or research; however, they do not support concrete conclusions. Concrete conclusions must be substantiated by facts, including evidence. In the instant, while the general direction of research may be outlined for the skilled artisan, the skilled artisan would not readily be able to practice the claimed invention without the undue burden of experimentation. The path that the skilled artisan must take in his research is marked with many challenges that are recognized in the art, including the complex nature of oligonucleotides containing CpG motif and the complexity of the immune system, including the Th1 type immune response and the functional characteristics of its associated cytokines. Hence, in view of the lack of any guidance in the specification concerning the effective use of oligonucleotides to suppress RSV infection in a subject; the unpredictability of oligonucleotides containing CpG motif to stimulate specific immune response; and the inherent toxicity, the unclear pharmacological behavior, and the pleiotropic effects of cytokines; the skilled artisan would not be able to reasonably practice the claimed invention without an undue burden experimentation. Thus, the claims are rejected under 35 U.S.C § 112, 1st paragraph for failing to comply with the enablement requirement.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. In response to the double patenting rejections provided below, Applicant submits that the rejections will be addressed upon the indication of allowable subject matter.

Applicant's submission has been requested. Until the rejections are properly addressed, the rejections will remain in the record.

7. Claims 1-5, 8-10 and 16-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 11 of copending Application No. 10/898512. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

The instant patent application is directed to a method of suppressing a respiratory syncytial virus (RSV) infection in an individual who has been exposed to RSV with the administration of a composition comprising an immunostimulatory sequence.

The conflicting patent application is directed to a method of reducing a symptom of a virus infection in an individual who has been exposed to a virus with the administration of a composition comprising an immunostimulatory sequence, wherein the sequence comprises a 5'-CG pyrimidine, pyrimidine, CG-3' motif.

The difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application require the sequence comprises a 5'-CG pyrimidine, pyrimidine, CG-3' motif. However, this sequence is encompassed by the generic ISS sequence language that is recited in the broadest claim of the instant patent application.

The difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not specify the virus in which the individual is infected. However, it is evident that by "viral infection", Applicant intends to encompass RSV infection. See paragraphs [0043-0044, and 0048] of the conflicting patent application's PreGrant publication, U.S. PreGrant Publication No. 20050059626.

The difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application are specifically directed at the reducing the severity of the symptoms of a virus infection. However, it is noted that by the recitation "suppressing" viral infection, as recited in claim 1 of the instant patent Application, Applicant also intends to encompass the reducing the severity of the symptoms of a virus infection. See lines 3-16 on page 11 of the instant patent application. Specifically, at the cited passage, Applicant notes that "suppressing" viral infection indicates any aspect of viral infection, such as viral replication, time course of infection, amount (titer) of virus, lesions, and/or one or more symptoms curtained, inhibited or reduced in an individual or a population of individuals treated with an ISS-containing polynucleotide in accordance with the invention as compared to an aspect of viral infection in an individual or population of individuals not treated in accordance of the invention. The specification continues by disclosing that a reduction of viral titer includes, but is not limited to, elimination of the virus from an infected site or individual.

The other notable difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not limit the length of the ISS sequence to greater than 6 and less than about 200 nucleotides in length. However, it is clear in specification of the conflicting patent application that by ISS, the sequence has to be greater than 6 nucleotides in length. See paragraph [0081 of the conflicting patent application's PreGrant publication, U.S. PreGrant Publication No. 20050059626.

The other notable difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not specify the individual to be a human. However, it is noted that by the recitation "individual", Applicant intended to encompass a human. See paragraph [0063] of the conflicting patent application's PreGrant publication, U.S. PreGrant Publication No. 20050059626.

The difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not negate the administration of an immunostimulatory cytokine and an adjuvant with the administration of the ISS. However, it should be noted here that the claims the conflicting patent application does not require the co-administration of an immunostimulatory cytokine and an adjuvant with the administration of the ISS.

The difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not require the administration to be at the nasal passages or at the lung. However,

due to the nature of the virus, respiratory virus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to have targeted the nasal passages and lungs of individuals that are exposed or infected with a respiratory virus. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to treat the infection directly at the site of infection.

The last difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not require the ISS composition to comprise a modified phosphate backbone. However, at the time the invention was made, it is well known in the art that nucleic acid sequence having a phosphorothioate backbone is more resistant to nuclease degradation than nucleic acid sequence having natural phosphodiester backbone. Thus, it would have been prima facie obvious for one of ordinary skill in the art to modify the natural phosphodiester backbone of the nucleic acid sequence to a phosphorothioate backbone. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to extend the half-life of the nucleic acid sequence.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 1-5, 8-10 and 16-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No. 10/426237. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

The instant patent application is directed to a method of suppressing a respiratory syncytial virus (RSV) infection in an individual who has been exposed to RSV with the administration of a composition comprising an immunostimulatory sequence.

The conflicting patent application is directed to a method of suppressing a respiratory virus infection in an individual who has been exposed to RSV with the administration of a composition comprising an immunostimulatory sequence, wherein the sequence comprises a 5'-CG-3' motif.

The notable difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not refer to RSV as the respiratory virus infection. However, it is noted that by the recitation "respiratory virus infection", Applicant intended to encompass RSV. See paragraph [0028] of the conflicting patent application's PreGrant publication, U.S. PreGrant Publication No. 20040009942.

The other notable difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not limit the length of the ISS sequence to greater than 6 and less than about 200 nucleotides in length. However, it is clear in specification of the conflicting patent application that by ISS, the sequence has to be greater than 6 nucleotides in length. See paragraph [0058] of the conflicting patent application's PreGrant publication, U.S. PreGrant Publication No. 20040009942.

The other notable difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not specify the individual to be a human. However, it is noted that by the recitation "individual", Applicant intended to encompass a human. See paragraph [0041] of the conflicting patent application's PreGrant publication, U.S. PreGrant Publication No. 20040009942.

The difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not negate the administration of an immunostimulatory cytokine and an adjuvant with the administration of the ISS. However, it should be noted here that the claims the conflicting patent application does not require the co-administration of an immunostimulatory cytokine and an adjuvant with the administration of the ISS.

The difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent application do not require the administration of the ISS composition to the lung. However, due to the nature of the virus, respiratory virus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to have targeted the lungs of individuals that are exposed or infected with a respiratory virus. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to treat the infection directly at the site of infection.

The last difference between the claims of the conflicting patent application and the claims of the instant patent application is: The claims of the conflicting patent

application do not require the ISS composition to comprise a modified phosphate backbone. However, at the time the invention was made, it is well known in the art that nucleic acid sequence having a phosphorothioate backbone is more resistant to nuclease degradation than nucleic acid sequence having natural phosphodiester backbone. Thus, it would have been prima facie obvious for one of ordinary skill in the art to modify the natural phosphodiester backbone of the nucleic acid sequence to a phosphorothioate backbone. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to extend the half-life of the nucleic acid sequence.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The above double patenting rejection(s) is, in part, based on the specification of a previously issued patent, rather than the claims. In support of the use of this material, the examiner notes the following excerpt from MPEP section 804 II(B)(1):

> When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. This does not mean that one is precluded from all use of the patent disclosure.
>
> The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the

> invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

Thus, the courts have held that it is permissible to use the specification in determining what is included in, and obvious from, the invention defined by the claim on which the rejection is based. This is true even where elements are drawn from the specification describing the claimed invention which are not elements in the claim itself.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Emily M. Le
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Art Unit 1648

E.Le